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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,376	10/11/2001	Chad A. Mirkin	00-713-i12	9821

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Emily Miao
McDonnell Boehnen Hulbert & Berghoff
32nd Floor
300 S. Wacker Drive
Chicago, IL 60606

EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,376	MIRKIN ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *237-265 and 433-441* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *237-265 and 433-441* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/6/03 & 1/31/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' After-final response, filed on November 6, 2003. Currently, claims 237-265 and 433-441 are pending.

2. The examiner for this application has changed. This action contains new grounds of rejection, not necessitated by Applicants' amendments. Accordingly, this action is made NON-FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Priority

3. Applicants' claim to priority has been acknowledged. However, the priority established for the claims is as follows:

Claims 237-242 have priority to US Provisional Application No. 60/031,809, filed on 07/29/1996.

Claims 243-265 and 433-441 have priority to US Application No. 09/603,830, filed on 06/26/2000. There does not appear to be any support for Claims 243-265 and 433-441 in US Application Nos. 09/344,667, 09/240,755, PCT/US97/12783, or 60/031,809. If Applicants' traverse this assertion, Applicants' are respectfully requested to point out with specificity (by page and line number) where there is support for Claims 243-265 and 433-441 in these earlier filed applications.

Terminal Disclaimer

4. The terminal disclaimer filed on November 6, 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. application numbers 09/957,313, 09/976,577, 09/976,378, 09/975,062, 09/976,617, 09/974,007, 09/973,638, 09/973,788 has been reviewed and is accepted. The terminal disclaimer has been recorded. It is also noted that the terminal disclaimer for U.S. Patent Number 6,417,340 was not received. It is suggested that Applicants re-send the terminal disclaimer for this patent. Accordingly, the obviousness-type double patenting rejection with respect to this patent is maintained in view of the non-receipt and non-entry of the terminal disclaimer.

Information Disclosure Statement

5. The information disclosure statements filed on November 6, 2003 and January 31, 2002 have been considered (see enclosed signed PTO-1449s). However, it is noted, the non-patent literature references appear to have not been received by the PTO. It is respectfully requested that Applicants' resubmit the non-patent literature references.

Statutory Double Patenting

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 433 and 437-441 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 21-25 of prior U.S. Patent No. 6,582,921. This is a double patenting rejection.

Claims 21-25 of USPN 6,582,921 recite,

> 21. A nanoparticle having one or more types of oligonucleotides bound thereto, at least one type of oligonucleotides having a sequence that is complementary to at least a portion of a nucleic acid target, wherein in the presence of said nucleic acid target and under hybridization conditions, the nanoparticle having oligonucleotides bound thereto form a complex with said nucleic acid target, the nanoparticle-nucleic acid target complex having a sharp melting profile and an increased melting temperature, relative to a melting profile and a melting temperature of an analogous complex formed with said nucleic acid target and an unlabeled or fluorophore-labeled oligonucleotide having a sequence identical to the oligonucleotides bound to the nanoparticics, to allow for selective discrimination of a single nucleotide insertion, deletion, or mismatch in said nucleic acid target under stringent hybridization conditions, whereby the stringency of said hybridization conditions are higher than those possible for said analogous complex.
>
> 22. The nanoparticles of claim 21, wherein the nanoparticles are metallic nanoparticles, semiconductor nanoparticles, or a combination thereof.
>
> 23. The nanoparticle of claim 21, wherein the nanoparticles are made of a noble metal.
>
> 24. The nanoparticle of claim 23, wherein the nanoparticles are made of gold.
>
> 25. The nanoparticle of claim 21, wherein the oligonucleotides, nanoparticles, or both bear functional groups for attachment of the oligonucleotides to the nanoparticles.

Accordingly, the '921 claims claim the same invention as instant claims 433 and 437-441.

8. Claims 237-265 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 237-265 and 433-446 of copending Application No. 09/974,007. This

is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

9. Claims 237-242 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 237-242 of copending Application No. 09/976,577. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

10. Claims 433 and 437-441 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 454-456 of copending Application No. 10/410,324. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Non-Statutory Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 237, 241-243, 251-253 and 264-265 are rejected under the judicially created doctrine of double patenting over claims 1-4 of USPN 6,417,340 (previously cited). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-4 of USPN 6,417,340 are drawn to a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

Specifically, the claims of '340 recite,

1. An aggregate probe comprising first and second types of nanoparticles having a first type of oligonucleotides attached thereto, the first type of nanoparticles having a second type of oligonucleotides attached thereto and the second type of nanoparticles having a third type of oligonucleotides attached thereto, the first type of oligonucleotides having a sequence complementary to a portion of the sequence of a nucleic acid, the second type of oligonucleotides having a sequence complementary to at least a portion of the sequence of the third type of oligonucleotides, wherein the nanoparticles are bound to each other as a result of the hybridization of some of the oligonucleotides attached to said nanoparticles.

2. An aggregate probe comprising first, second and third types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides attached to the first type of nanoparticles having a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the second type of nanoparticles, the oligonucleotides attached to the second type of nanoparticles having a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the first type of nanoparticles, and the third type of nanoparticles having two types of oligonucleotides attached thereto, the first type of oligonucleotides having a sequence complementary to a portion of the sequence of a nucleic acid, and the second type of oligonucleotides having a sequence complementary to at least a portion of the sequence of the oligonucleotides attached to the first or second type of nanoparticles, wherein the nanoparticles are bound to each other as a result of the hybridization of some of the oligonucleotides attached to said nanoparticles.

3. The aggregate probe of claims 1 or 2, wherein the nanoparticles are metallic nanoparticles, semiconductor nanoparticles, or a combination thereof.

4. The aggregate probe of claims 1 or 2, wherein the nanoparticles are gold nanoparticles.

Accordingly, because the claims of '340 are a species of the instant claims, the claims of '340 are obvious to the instant claims.

13. Claims 237 and 241-242 are rejected under the judicially created doctrine of double patenting over claim 1 of USPN 6,361,944 (cited in the IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of claim 1 of

USPN 6,361,944 uses a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

Specifically, Claim 1 of '944 recites,

A method for detecting a nucleic acid having a first and second portion comprising: (a) providing a substrate having attached thereto oligonucleotides complementary to the first portion of the nucleic acid; (b) providing gold nanoparticles having bound thereto by way of sulfur linkages oligonucleotides complementary to the second portion of the nucleic acid; wherein the oligonucleotides complementary to the second portion of the nucleic acid to be detected are bound to the gold nanoparticle in an aging process comprising fire binding oligonucleotides to the gold nanoparticle in water and then binding additional oligonucleotides to the gold nanoparticle in a salt solution; (c) contacting the substrate and gold nanoparticles provided in (a) and (b), respectively, with the nucleic acid under hybridizing conditions to bind the nucleic acid to the substrate and the gold nanoparticles; and (d) detecting the gold nanoparticles bound to the nucleic acid bound to the substrate.

Accordingly, because Claim 1 of '944 uses a species of the instant claims, the claims of '944 are obvious over the instant claims.

14. Claims 237 and 241-242 are rejected under the judicially created doctrine of double patenting over claims 1-2 and 11-12 of USPN 6,495,324. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of claim 1 of USPN 6,495,324 uses a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

Specifically, Claim 1 of '324 recites,

A method of detecting nucleic acid having at least two portions comprising: contacting a nucleic acid to be detected with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid; contacting said nucleic acid bound to the substrate with liposomes having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the liposomes with said nucleic acid; providing an aggregate probe comprising at least two types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides attached to the

nanoparticles having first and second ends wherein the first ends are attached to the nanoparticles and the second ends are not attached to the nanoparticles, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a hydrophobic group attached to the second end; contacting the liposomes bound to the substrate with the aggregate probe under conditions effective to allow attachment of the oligonucleotides on the aggregate probe to the liposomes as a result of hydrophobic interactions; and observing a detectable change.

Accordingly, because Claim 1 of '324 uses a species of the instant claims, the claims of '324 are obvious over the instant claims.

15. Claims 237, 241-243, 251-253 and 264-265 are rejected under the judicially created doctrine of double patenting over claims 1-2, 8-10, 22-26 and 31-34 of USPN 6,506,564. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of USPN 6,506,564 comprise a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

For example, Claim 31 of '564 recites,

A kit comprising at least one container, the container holding a composition comprising at least two types of gold nanoparticles having oligonucleotides attached thereto, the oligonucleotides on the first type of nanoparticles having a sequence complementary to the sequence of a first portion of a nucleic acid, the oligonucleotides on the second type of nanoparticles having a sequence complementary to the sequence of a second portion of the nucleic acid, wherein the oligonucleotides are attached to the nanoparticles by contacting the oligonucleotides with the nanoparticles in the presence of water for a sufficient period of time to allow at least some of the oligonucleotides to bind to the nanoparticles and in the presence of a salt solution for an additional period of time sufficient to allow additional oligonucleotides to bind to the nanoparticles.

Accordingly, because the claims of '564 use a species of the instant claims, the claims of '564 are obvious over the instant claims.

16. Claims 433 and 437-441 are rejected under the judicially created doctrine of double patenting over claims 1-10, 13, 16-19 of USPN 6,582,921. Although the conflicting claims are

not identical, they are not patentably distinct from each other because the methods of USPN 6,582,921 use a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

For example, Claim 1 of '921 recites,

A method of detecting one or more nucleic acid targets, each having at least two portions comprising: providing a substrate having one or more types of first nanoparticles attached thereto, each type of first nanoparticles having oligonucleotides attached thereto, the oligonucleotides of each type of first nanoparticles having a sequence complementary to a first portion of the sequence of a specific nucleic acid target to be detected; contacting one or more nucleic acid targets with the first nanoparticles attached to the substrate under conditions effective to allow hybridization of the oligonucleotides on the first nanoparticles with said nucleic acid targets; providing one or more types of second nanoparticles having oligonucleotides attached thereto, the oligonucleotides of each type of second nanoparticles having a sequence complementary to one or more other portions of the sequence of said nucleic acid target to be detected; contacting said nucleic acid targets bound to the substrate with one or more types of second nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the second nanoparticles with said nucleic acid targets; and observing a detectable change, wherein in the presence of said one or more nucleic acid targets and under hybridization conditions, said nanoparticles having oligonucleotides bound thereto form complexes with said nucleic acid targets, the resulting nanoparticle-nucleic acid target complexes having a sharp melting profile and an increased melting temperature, relative to a melting profile and a melting temperature of analogous complexes formed with said nucleic acid targets and an unlabeled or fluorophore-labeled oligonucleotides having a sequence identical to the oligonucleotides bound to the nanoparticles, to allow for selective discrimination of a single nucleotide insertion, deletion, or mismatch in said nucleic acid targets under stringent hybridization conditions, whereby the stringency of said hybridization conditions are higher than those possible for said analogous complexes.

Accordingly, because the claims of '921 use a species of the instant claims, the claims of '921 are obvious over the instant claims.

17. Claims 237 and 241-242 are rejected under the judicially created doctrine of double patenting over claims 1-2 and 5-6 of USPN 6,610,491. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of USPN

6,610,491 comprise a species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

For example, Claims 1-2 of '491 recite,

1. A method of detecting nucleic acid having at least two portions comprising: contacting a nucleic acid to be detected with a substrate having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid; contacting said nucleic acid bound to the substrate with liposomes having oligonucleotides attached thereto, the oligonucleotides having a sequence complementary to a portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the liposomes with said nucleic acid; providing an aggregate probe comprising at least two types of nanoparticles having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, at least one of the types of nanoparticles of the aggregate probe having oligonucleotides attached thereto which have a hydrophobic group attached to the end not attached to the nanoparticles; contacting the liposomes bound to the substrate with the aggregate probe under conditions effective to allow attachment of the oligonucleotides on the aggregate probe to the liposomes as a result of hydrophobic interactions; and observing a detectable change.

2. The method of claim 1 wherein the nanoparticles in the aggregate probe are made of gold.

Accordingly, because the claims of '491 use a species of the instant claims, the claims of '491 are obvious over the instant claims.

18. Claims 237, 241-243, 251-253, 264-265, 433, 437 and 440 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 8, 23-24, 29, 42, 113 of copending Application No. 09/923,625. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '625 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 237-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433-439, 449-453, 461-486, 496-500 and 508-521 of copending Application No. 09/957,318. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of '318 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 237, 241-243, 251-253, 264-265, 433 and 438-441 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 80-83 and 438-439 of copending Application No. 09/966,312. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '312 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

21. Claims 237, 241-243, 251-253 and 264-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 85-89, 150-154 and 433-436 of copending Application No. 09/967,409. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and

kits of '409 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

22. Claims 237, 241-243, 251-253 and 264-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433, 443-445, 454-455, 464, 473, 474, 484, 493, 502, 512 of copending Application No. 09/974,500. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of '500 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Claim 237 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 155 and 170 of copending Application No. 09/975,384. Although the conflicting claims are not identical, they are not patentably distinct from each other because the kits of '384 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

24. Claims 237, 241-243, 251-253 and 264-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433-436, 446-448 and 458-461 of copending Application No. 09/975,498. Although the conflicting

claims are not identical, they are not patentably distinct from each other because the methods of '498 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claims 237, 243 and 253 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433, 446 and 461-486 of copending Application No. 09/975,059. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '059 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 237-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433 and 443-461 of copending Application No. 09/976,601. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of '601 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Claims 237, 241 and 242 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433, 435, 437, 445, 454-457 and 460-465 of copending Application No. 10/410,324. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of

'324 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

28. Claims 237-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433-462 of copending Application No. 09/976,971. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods and kits of '971 comprise species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

29. Claims 237-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 433-435, 489-500, 508-522, 531-536, 546-556 of copending Application No. 09/976,863. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '863 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

30. Claims 237-265 and 433-441 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 8, 11, 433, 435, 436 and 442-444 of copending Application No. 09/981,344. Although the conflicting

claims are not identical, they are not patentably distinct from each other because the methods of '344 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

31. Claims 237-265 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 407, 409-410, 433, 435-436, 442-445, 450, 452-453, 466-483 of copending Application No. 09/976,900. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '900 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

32. Claims 237-265 and 433-441 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 243-265 and 433-446 of copending Application No. 09/976,618. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of '618 use species of the instantly claimed genus of nanoparticles comprising oligonucleotides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

34. Claims 237-241, 243-246, 248-251, 253-257 and 259-264 are rejected under 35 U.S.C. 102(b) as being anticipated by Coffer et al. (Nanotechnology (1992) 3: 69-76).

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is noted that, the recitation of "the oligonucleotides...so that the nanoparticles are stable" is not limiting, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least some" of the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to claims 243-265, the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad any encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to the nanoparticle.

Coffer teaches the attachment of an oligonucleotide to a semiconductor nanoparticle at a surface density sufficient so that the nanoparticles are stable (see pages 69-72 and 75).

35. Claims 237-240, 243-246, 248-250, 253-257 and 259-263 are rejected under 35 U.S.C. 102(b) as being anticipated by Chavany et al. (Pharmaceutical Research (1994) 11(9): 1370-1378).

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is noted that, the recitation of "the oligonucleotides...so that the nanoparticles are stable" is not limiting, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least some" of the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to claims 243-265, the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad any encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to the nanoparticle.

Chavany teaches the attachment of an oligonucleotide to a nanoparticle at a surface density sufficient so that the nanoparticles are stable (see pages 1370-1372, 1375 and 1377).

36. Claims 237-265 are rejected under 35 U.S.C. 102(e) as being anticipated by Kossovsky et al. (USPN 5,460,831).

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is noted that, the recitation of "the oligonucleotides...so that the nanoparticles are stable" is not limiting, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least some" of the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to claims 243-265, the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad any encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to the nanoparticle.

Kossovsky teaches the attachment of an oligonucleotide to a gold nanoparticle at a surface density sufficient so that the nanoparticles are stable (see abstract, cols. 3-4 and Examples 1-13).

37. Claims 237-265 are rejected under 35 U.S.C. 102(e) as being anticipated by Kausch et al. (USPN 5,665,582).

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is noted that, the recitation of "the oligonucleotides...so that the nanoparticles are stable" is not limiting, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least some" of the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to claims 243-265, the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad any encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to the nanoparticle.

Kausch teaches the attachment of an oligonucleotide to a gold nanoparticle at a surface density sufficient so that the nanoparticles are stable (see abstract, cols. 4-10, 17-19, 24 and Examples 1, 2 and 4-8).

38. Claims 237-265 are rejected under 35 U.S.C. 102(e) as being anticipated by Yguerabide et al. (6,214,560).

It is noted that the claims do not limit the attachment of the oligonucleotide, and therefore, the claim reads on an indirect attachments (e.g., through a moiety). Furthermore, it is

noted that, the recitation of "the oligonucleotides...so that the nanoparticles are stable" is not limiting, since stability would likely depend on external conditions (e.g., temperature, aqueous conditions, etc.), and presumably, as long as the oligonucleotide is attached either directly or indirectly, the oligonucleotides would be present at a surface density sufficient so that the nanoparticles are stable. In addition, since only "at least some" of the oligonucleotides have a sequence complementary to "at least a portion" of the sequence of a another nucleic acid or another oligonucleotide, the oligonucleotide can comprise any nucleic acid sequence. Furthermore, with respect to claims 243-265, the recitation of "recognition oligonucleotide", "spacer portion" and "diluent oligonucleotide" are only limiting to their specific definitions given in the specification (see page 22, lines 2-6). These definitions are very broad any encompass any nucleotide sequence. Accordingly, the claims have been interpreted as being drawn to a nanoparticle comprising an oligonucleotide, wherein the oligonucleotide is either directly or indirectly attached to the nanoparticle.

Yguerabide et al. discloses a method of light illumination and detection named "DLASLPD" (direct light angled for scattered light only from particle detected), which is an analyte assay using gold particulate label for specific detection of one or more analytes in a sample. One or more analytes in a sample can be detected and measured by detection and/or measurement of one or more of the specific light scattering properties of metal-like particles. (Summary of the Invention). For example, a certain nucleic acid analyte is composed of about 100 nucleic acid bases and is present in a sample. The sample is prepared so that this nucleic acid is in a single stranded form. Then two or more unique single-stranded "probe" nucleic acid sequences are added to the sample where these different probes bind to different regions of the

target strand. Each of these probes has attached to one or more particles (col. 74). Further, the particles can form different types of aggregates that can be detected visually or instrumentally in a microscope or through macroscopic observation or measurements without having to separate free from analyte bound particles. Low particle surface density (less than 0.1 particles per mu^2) on a spot and high particle surface density (greater than 0.1 particles per mu^2) on a spot are also disclosed which are viewed to be inclusive of the instant claims.

In certain analytical and diagnostic assays, it may be preferable to increase the detectability of the scattered light properties of the particles so that very simplified or no detection instrumentation is required. By use of the appropriate molecular recognition binding-pairs and particles it is possible to significantly increase the level of detection sensitivity. Single-stranded homopolymer sequences, avidin-biotin, streptavidin-biotin, and other binding-pair systems can be used to "chain-together" and "build-up" many particles (col. 73-76).

The reference describes methods of attachment of substances to particles and other surfaces. In this method of attaching substances to particles or other surfaces, a two step approach which involves the use of base material molecules is used. Suitable base material molecules are any substance which can approach and interact with the surface by adsorption or other chemical process, and have accessible functional groups to which additional substances, as for example, binding agents can be attached. As an example, the reference has used a derivative of a polyethylene glycol. The properties of this molecule allow for its use as a base material molecule. Each molecule of this polymer has four amine groups, which can serve as linkage sites for the conjugation of additional substances. The hydrophobic backbone of the polyethylene derivative interacts with the particle and is attached to the particle

surface by adsorption or some other process. This interaction is very strong. The amine groups do not appear to interact with the particle surface and are accessible as conjugation sites for the attachment of additional substance, such as, binding agents. Using this polymer as the base molecule they have prepared two different types of particle-binding agent reagents. One reagent contains biotin groups as binding agents and the other particle-binding agent reagent was made to contain single-stranded nucleic acids as binding agents. The biotin used for attachment was a chemically modified form where it will covalently link to amine groups. For the nucleic acids, the 5' ends were chemically modified so that they would chemically react with the amine groups. Linker arms of various lengths and composition can also be incorporated into the molecular structure. For example, a small molecular weight base material molecule an be used where it's molecular structure is optimized for attachment to the particle or surface, attachment of most any substance to it with any desired orientation, and with a high level of binding activity. As an example, a linear polypeptide twenty amino acids in length is chemically modified at one terminus by the addition of disulfide or thiol chemical groups. The native polypeptide is composed of amino acids such that the polypeptide chain will not interact with the surface except through the chemically modified end. At the other terminus a free amino group exists, or alternatively, has been chemically modified for a desired conjugation process such that most any substance can be attached at this position. This low molecular weight base material molecule then is used in one or more variations of the methods as described herein. (col. 77-81). The polyethylene glycol or the polypeptide is viewed to be inclusive of the spacer portion of instant claim 243 for example. And the amine group is viewed to be inclusive of the functional group.

Conclusion

39. No Claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

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Alexander H. Spiegler
March 8, 2004

CARLA J. MYERS
PRIMARY EXAMINER